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MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/826,966	MCSWIGGEN ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,14-21,30,31 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,14-21,30,31 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *4/16/04, 9/20/04, and 10/2/06* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :August 13, 2004 and June 13, 2005 .

DETAILED ACTION

This Office Action is a response to Applicant's Amendment and Election filed October 2, 2006.

Claims 2, 4-13, 22-29 and 32 have been canceled. Claims 1, 3, 14-21, 30, and 31 have been amended. New claim 33 is acknowledged.

Claims 1, 3, 14-21, 30, 31, and 33 are pending in the instant application.

Claims 1, 3, 14-21, 30, 31, and 33 have been examined on the merits.

Election/Restrictions

The previous Restriction Requirement mailed August 28, 2006 is moot in view of Applicant's Amendment filed October 2, 2006 to cancel claim 2.

Information Disclosure Statement

Applicant's information disclosure statement filed August 13, 2004 is acknowledged. The submission is not fully compliant with the provisions of 37 CFR §1.97, which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It is noted that an English translation of European Document 1144623 B1 has not been provided. Therefore, European Document 1144623 has not been considered on the merits. Also, only the

Abstracts of WO 01/42443, WO 01/70944, WO 02/55692, and WO 02/55693 have been considered since the remainder of the WO Documents have not translated in English. Accordingly, the Examiner has considered the information disclosure statement, and a signed copy is enclosed herewith. However, European Document 1144623 B1 has been lined through, indicating that the reference has not been considered, and it has been indicated that only the Abstracts of WO 01/42443, WO 01/70944, WO 02/55692, and WO 02/55693 have been considered.

Applicant's information disclosure statement filed June 13, 2005 is acknowledged. The submission is in compliance with the provisions of 37 CFR §1.97. Accordingly, the Examiner has considered the information disclosure statement, and a signed copy is enclosed herewith.

Priority

It is noted that the instant application claims priority to a laundry list of U.S. Provisional Applications and pending U.S. Patent Applications. First, the reference should be updated to reflect applications for patents that are pending or that have been abandoned. Second, due to the voluminous nature and number of the applications to which priority is claimed, Applicant are requested to point out with particularity where support for the instantly claimed invention may be found in one or more of the prior filed applications to which benefit is claimed, since such support is not readily apparent in the priority documents.

The later-filed application must be an application for a patent for an invention

which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

It is further noted the instant claims have been amended and are currently drawn to a chemically modified siNA molecule comprising a sense strand and an antisense strand, wherein the antisense strand is complementary to a hepatitis B virus (HBV) comprising SEQ ID NO:674. The Examiner would like to point out that Applicants contend that SEQ ID NO:674 represents GenBank entry AF100308 as disclosed at page 230 of the instant specification (see Applicant's Remarks filed October 2, 2006 at page 7, last paragraph). At the outset, it is immediately noticed that the sequence of GenBank Accession Number AF100308 contains thymine residues, where SEQ ID NO:674 of the instant application has substituted the thymine residues with uracil residues.

The instant application claims priority to a number of parent applications including Provisional Applications 60/358,580, 60/363,124, and 60/386,782, filed February 20, 2002, March 11, 2002, and June 6, 2002, respectively. Now then, referring to Provisional Application 60/358,580, it is noted that the Examiner cannot find support for SEQ ID NO:674 or GenBank Accession Number AF100308. While the Provisional Application has support for GenBank Accession Number AF100308.1 (see

page 54, first full paragraph), GenBank Accession Number AF100308 is not specifically supported.

Next, referring to Provisional Application 60/363,124, it is noted that the Examiner cannot find support for SEQ ID NO:674 or GenBank Accession Number AF100308. While the Provisional Application has support for GenBank Accession Number AF100308.1 (see page 63, last paragraph), GenBank Accession Number AF100308 is not specifically supported.

Next then, referring to Provisional Application 60/386,782, it is similarly noted that the Examiner cannot find support for SEQ ID NO:674 or GenBank Accession Number AF100308. While the Provisional Application has support for GenBank Accession Number AF100308.1 (see page 55, second paragraph), GenBank Accession Number AF100308 is not specifically supported.

In summary, Applicants claim priority to a number of parent applications, however, none of the parent applications appear to have support for a chemically modified siNA molecule comprising a sense strand and an antisense strand, wherein the antisense strand is complementary to a hepatitis B virus (HBV) comprising SEQ ID NO:674 as instantly claimed. In this regard, the instant claims have been afforded priority to the filing date of the instant application, which is April 16, 2004.

If Applicants believe that they are entitled to an earlier priority date, the Examiner urges Applicant to specifically point where support can be found for SEQ ID NO:674 or GenBank Accession Number AF100308 in any other applications Applicants claim priority to.

Specification

The amendment filed October 2, 2006 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: In the Amendment filed October 2, 2006, Applicants have submitted a new sequence listing in which SEQ ID NO:674 has been added. Applicants contend that SEQ ID NO:674 represents GenBank entry AF100308 as disclosed at page 230 in the instant specification (see Applicant's Remarks filed October 2, 2006, at page 7, last paragraph). At the outset, it is noted that page 230 of the instant specification recites, "GenBank Accession No. AF100308.1". Nowhere on page 230 of the instant specification is "GenBank Accession Number AF100308" recited. It is further noted that the sequence of GenBank entry AF100308 was submitted and made of record on the information disclosure statement filed August 13, 2004. Comparing GenBank entry AF100308 with SEQ ID NO:674 of the instant application, it is immediately noticed that the sequence of the Accession Number contains thymine residues, where SEQ ID NO:674 has substituted the thymine residues with uracil residues.

In summary, the instant specification does not support GenBank Accession Number AF100308. Furthermore, GenBank Accession Number NM_003376 and newly submitted sequence SEQ ID NO:674 are not the same sequence since one is a DNA sequence and the other is an RNA sequence. In this regard, SEQ ID NO:674 appears to be new matter.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

Claim 31 is objected to because of the following informalities: Claim 31 incorrectly recites, "A composition comprising the siNA molecule of claim 1 in pharmaceutically acceptable carrier or diluent". It appears that the claim should correctly recite, "A composition comprising the siNA molecule of claim 1 in **a** pharmaceutically acceptable carrier or diluent". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 33 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 33 is indefinite because it recites the limitation, "wherein said chemical modification". There is insufficient antecedent basis for this limitation in the claim because claim 1, from which claim 33 depends recites, "chemically modified". Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 14-21, 30, 31, and 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The instant claims are drawn to a chemically modified siNA molecule comprising a sense strand and an antisense strand, wherein the antisense strand is complementary to a hepatitis B virus (HBV) comprising SEQ ID NO:674. It is noted that SEQ ID NO:674 was added to the sequence listing in the Amendment filed October 2, 2006. The Examiner would like to point out that Applicants contend that SEQ ID NO:674 represents GenBank entry AF100308 as disclosed at page 230 in the instant specification (see Applicant's Remarks filed October 2, 2006, at page 7, last paragraph). At the outset, it is noted that page 230 of the instant specification recites, "GenBank Accession No. AF100308.1". Nowhere on page 230 of the instant specification is "GenBank Accession Number AF100308" recited. It is further noted that GenBank entry AF100308 was submitted and made of record on the information disclosure statement filed August 13, 2004. Comparing GenBank entry AF100308 with SEQ ID NO:674 of the instant application, it is immediately noticed that the sequence of the Accession

Number contains thymine residues, where SEQ ID NO:674 has substituted the thymine residues with uracil residues.

In summary, the instant specification does not support GenBank Accession Number AF100308. Furthermore, GenBank Accession Number NM_003376 and newly submitted sequence SEQ ID NO:674 are not the same sequence since one is a DNA sequence and the other is an RNA sequence. In this regard, SEQ ID NO:674 appears to be new matter.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 14-21, 30, 31, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over GenBank Accession Number AF100308 (submitted and made of record on the information disclosure statement filed August 13, 2004), in view of Hamasaki et al. (FEBS Letters, 2003 Vol. 354 :51-54), Braasch et al. (Biochemistry, 2003 Vol. 42 :7967-7975), Elbashir et al. (submitted and made of record on the information disclosure statement filed August 13, 2004), Matulic-Adamic et al. (US

Patent No. 5,998,203), and/or Parrish et al. (submitted and made of record on the information disclosure statement filed August 13, 2004).

Applicant is reminded that the instant application has been afforded priority to the filing date of the instant application, which is April 16, 2004. For further explanation, see the discussion above under the heading "Priority".

Claim 1 is drawn to a chemically modified siNA molecule comprising a sense strand and an antisense strand, wherein the antisense strand is complementary to a hepatitis B virus (HBV) comprising SEQ ID NO:674, wherein about 100% of nucleotide positions in one or both strands of said siNA molecule are chemically modified. Clams 3, 14-21, 30, 31, and 33 are dependent on claim 1 and include all the limitations of claim 1 with the further limitations wherein said siNA molecules comprise ribonucleotides; wherein one or more purine or pyrimidine nucleotides are present on the sense strand; wherein the purine nucleotide is a 2'-deoxy purine and the pyrimidine nucleotide is a 2'-deoxy-2'-fluoro pyrimidine nucleotide; wherein the sense strand comprises a terminal cap moiety at the 5' or 3' end, or both; wherein said terminal cap moiety is an inverted deoxy abasic moiety; wherein the antisense strand comprises 2'-deoxy-2'-fluoro pyrimidine nucleotides; wherein the purine nucleotide on the antisense strand is a 2'-methyl purine nucleotide or a 2'-deoxy purine nucleotide; wherein the antisense strand comprises a phosphororthioate internucleotide linkage at the 3' end of the antisense strand; wherein the 5'-end of the antisense strand includes a terminal phosphate group; and a chemically modified siNA molecule comprising a sense strand and an antisense strand, wherein the antisense strand is complementary to a hepatitis B virus (HBV)

comprising SEQ ID NO:674, wherein about 100% of nucleotide positions in one or both strands of said siNA molecule are chemically modified in a pharmaceutically acceptable carrier or diluent.

Applicant is reminded that during patent examination, the claims are given the broadest reasonable interpretation consistent with the specification. See MPEP § 2111-2116.01. The term "about" has not been defined in the instant specification, therefore, the Examiner is interpreting the limitation, "about 100%" broadly to be at least 50%.

GenBank Accession Number AF100308 teaches the sequence of a human hepatitis B virus (HBV).

GenBank Accession Number AF100308 does not teach a short interfering nucleic acid (siNA) molecule that is complementary to a HBV, wherein about 100% of nucleotide positions in one or both strands of said siNA molecule are chemically modified.

Hamasaki et al. teach short interfering RNA-directed inhibition of hepatitis B virus replication (see Abstract). Specifically, Hamasaki et al. teach that transfection of human hepatoma cells with siRNA targeted to HBV reduced gene expression levels, viral protein, and replication (see Figures 2-4). Hamasaki et al. teach the siRNA were transfected using oligofectamine, which represents a pharmaceutical acceptable carrier.

Braasch et al. teach chemically-modified siRNAs (see Abstract). Specifically, Braasch et al. teach siRNAs wherein about 100% of the nucleotide positions in one of the strands are chemically modified with phosphorothioate linkages (see Figure 4). Braasch et al. also taught that the incorporation of phosphorothioate linkages stabilizes

RNA, and in this case, retains the ability to inhibit gene expression.

Elbashir et al. teach siRNAs, wherein each strand is 21-23 nucleotides in length and wherein at least 19 nucleotides of the sense strand are complementary to the antisense strand (see Abstract). Elbashir et al. teach modification of the internal nucleotides with 2'-deoxy or 2'-O-methyl modifications (see Abstract and Figure 4). Elbashir et al. teach that duplexes 21 nucleotides in length with 2 nt 3' overhangs were the most efficient triggers of sequence-specific mRNA degradation. Elbashir et al. teach 2'-deoxythymidine in the 3' overhang (see Figures 7 and 8). Elbashir et al. teach that a 5'-phosphate on the target-complementary strand of a siRNA duplex is required for siRNA function.

Matulic-Adamic et al. teach chemical modifications of double stranded nucleic acid structures (see Abstract). The enzymatic RNA molecules of Matulic-Adamic et al. are taught to be targeted to virtually any RNA transcript and achieve efficient cleavage (see column 1) and to be sufficiently complementary to a target sequence to allow cleavage. Matulic-Adamic et al. teach the incorporation of chemical modifications at the 5' and/or 3' ends of the nucleic acids to protect the enzymatic nucleic acids from exonuclease degradation, which improves the overall effectiveness of the nucleic acid, as well as facilitates uptake of the nucleic acid molecules (see column 2). Matulic-Adamic et al. teach base, sugar and/or phosphate modification, as well as terminal cap moieties at the 5'-cap, 3'-cap, or both. Specifically, 3'-phosphorothioates, inverted abasic moieties, and 2'-O-methyl modifications are utilized. Matulic-Adamic et al. teach 2'deoxy nucleotides and 2'-deoxy-2'-halogen nucleotides, wherein Br, CL and F are

representative halogens (see column 3, for example). The modifications can be in one or both of the strands and can be modifications of different types within the same structure.

Parrish et al. teach chemically synthesized double stranded siRNA molecules comprising various modifications in the sense or antisense strand, including 2'-deoxy-2'-fluoro modifications (see Figure 5). One or both strands comprise modifications. Parrish et al. teach that certain modifications were well tolerated on the sense, but not the antisense strand, indicating that the two trigger strands have distinct roles in the RNA interference process (see Summary).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a chemically modified siNA comprising a sense strand and an antisense strand, wherein the antisense strand is complementary to a HBV nucleotide sequence comprising SEQ ID NO:674 using the sequence taught by GenBank Accession Number AF100308, the motivation of Hamasaki et al., and following the methods of Elbashir et al., Matulic-Adamic et al., Parrish et al. It would have been obvious to have about 100% of the nucleotide positions in one of the strands be chemically modified using the teachings and motivation of Braasch et al. It would have been obvious to have the siNA comprised in a pharmaceutically acceptable carrier or diluent using the teachings and motivation of Hamasaki et al.

It would have been obvious to one of ordinary skill in the art at the time of filing to incorporate at least one 2'-O-methyl or 2'-deoxy-2-fluoro nucleotide modification into a chemically synthesized siNA molecule complementary to a HBV comprising SEQ ID

NO:674, since Elbashir et al., Matulic-Adamic et al., and Parrish et al. taught various modifications have been incorporated into double stranded nucleic acids to facilitate uptake of the nucleotide. It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate chemical modifications to about 100% of the nucleotide positions in one of the strands of the nucleic acid molecule since Braasch et al. taught that phosphorothioate linkages stabilize the nucleic acid, while maintaining the ability to inhibit gene expression. It would have been obvious to incorporate a terminal cap moiety on one of the ends of the sense strand since Matulic-Adamic et al. taught such modifications protect the nucleic acid from exonuclease degradation. It would have been obvious to incorporate a phosphororthioate internucleotide linkage at the 3' end of the antisense strand or a terminal phosphate group at 5'-end of the antisense strand since either Elbashir et al., Matulic-Adamic et al., and/or Parrish et al. teach such modifications protein the nucleic acid from nuclease attack.

One would have been motivated to incorporate at least one 2'-O-methyl or 2'-deoxy-2-fluoro nucleotide modifications into a chemically synthesized siNA molecule complementary to a HBV comprising SEQ ID NO:674 since these modifications were known in the art to add benefits to double stranded nucleic acids such as protection from exonuclease degradation and improve uptake of the nucleic acid, as taught by Elbashir et al., Matulic-Adamic et al., Parrish et al. It was well known in the art at the time of filing to incorporate two or more modifications, including 2'-O-methyl or 2'-deoxy-2-fluoro nucleotide modifications, into oligonucleotides, as evidenced by Elbashir et al., Matulic-Adamic et al., and Parrish et al. Elbashir et al. had demonstrated both 2'-deoxy

and 2'-O-methyl modifications of double stranded oligonucleotides at the time the invention was made. Matulic-Adamic et al. taught double stranded oligonucleotides comprising more than one specific type of modification. Additionally, Parrish et al. teach various modifications to double stranded duplexes and teach that different modifications are tolerated at different locations of the duplex. Elbashir et al. and Parrish et al. demonstrate the routine nature of testing various chemical modifications for optimization and stabilization of a double stranded duplex. The cited art demonstrates that the specific modifications were extensively described in the art. One of skill in the art would be motivated to test modifications that are known to benefit oligonucleotide delivery and apply each of them to a double stranded nucleic acid molecule in order to optimize delivery of the nucleic acid. One of skill in the art would be motivated to incorporate chemical modifications to about 100% of the nucleotide positions in one of the strands of the nucleic acid molecule since Braasch et al. taught that phosphorothioate linkages stabilize the nucleic acid, while maintaining the ability to inhibit gene expression. One of skill in the art would be motivated to have the siNA comprised in a pharmaceutically acceptable carrier or diluent to facilitate its delivery *in vitro* or *in vivo* as taught by Hamasaki et al.

There would be a reasonable expectation of success to apply each of the claimed modifications to the siNA molecules taught by Hamasaki et al. because the chemistry was well known to one of ordinary skill in the art at the time the invention was made (see Elbashir et al., Parrish et al., and Matulic-Adamic et al.) and merely selecting combinations of such modifications is considered a design choice. There would be a

reasonable expectation of success to apply chemical modifications to about 100% of the nucleotide positions in one strand of the siNA molecule since Braasch et al. taught siRNA comprising chemical modifications to about 100% of the nucleotide positions in one strand of the siNA molecule retain functionality. Modifications of double stranded ribonucleotides, including siNAs, was known to be successful in the art at the time the invention was made and therefore one would reasonably expect for such modifications to benefit the siNA as instantly claimed.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was filed.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

tcg
October 16. 2006